UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
ADDRESS: COMMISSIONER OF PATENTS AND TRADEMARKS
WASHINGTON, D.C. 20231

APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/788,552	02/21/2001	Serge Braun	032751-053	5627

21839 7590 08/12/2002

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	14

DATE MAILED: 08/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/788 552	BRAUN SERGE
Examiner	**Art Unit**
Ram Shukla	1632

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other *detailed action*

DETAILED ACTION

1. The Examiner prosecuting this application has been changed. Any inquiries relating to the examination of the application should be directed to Examiner Shukla, whereas any inquiries relating to formal matters should be directed to Ms. Jacobs, Patent Analyst. The phone numbers for Examiner Shukla and Patent Analyst Jacobs are provided at the end of this office action.

2. Amendments and response filed 5-15-02 have been received and entered.

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Applicants have not referenced the priority in the first sentence.

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in the instant application.The specification is objected to because the brief description of figure 2 does not match with the figure. Figure 2 has two panels A and B, however, the specification does not describe the panels A and B. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 45-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating multiple sclerosis, wherein a nucleic acid encoding beta-interferon comprising beta-interferon secretory signal is directly administered to muscle cells and a pharmaceutical composition comprising an effective amount of a nucleic acid encoding beta-interferon comprising beta-interferon secretory signal, wherein the composition is nucleic acid is DNA or naked DNA, wherein the DNA is associated with a

transfection-facilitating vehicle and wherein the transfection facilitating vehicle is selected from a list of cationic lipids, cationic polymers and polypeptides and wherein the pharmaceutical composition is suitable for injection, does not reasonably provide enablement for a method of treating any immune disease or any demyelinating disease or wherein the nucleic acid is administered by any route and other embodiments for reasons of record set forth in the previous office action of 1-15-02 and as discussed below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 5-15-02 have been fully considered but they are not persuasive. It is noted that in view of applicants arguments, the full lack of enablement rejection set forth in the previous office action has been modified to a scope rejection. Accordingly, only applicants' those arguments will be responded to which are directed to rejected embodiments. While applicants arguments are persuasive that EAE is a model for MS, applicants have not produced any evidence that EAE is the model for any immune disease. Applicants have listed numerous diseases as immune diseases, however, EAE is not a model for all these diseases. Next, while applicants arguments are persuasive to the extent that direct administration of the nucleic acid to muscles, as discussed in the previous office action, administration of a nucleic acid by any routes using any vectors was unpredictable at the time of the invention. Additionally, applicants do not teach as to how a viral particle would be used as a transfection vehicle. While it is known that a viral particle is a vector comprising a nucleic acid, it is not routine in the art to use viral particle as a transfecting vehicle as one would use a lipid in transfection. Regarding Applicants' arguments that gene therapy is a plausible treatment for MS and their citing of Ruffini et al does not provide support for any method of administration. Furthermore, the Ruffini et al used a specific method, which is not disclosed in the specification of the instant application, therefore,

Ruffini et al a post filing art can not be used to support the instant specification. Applicants have argued that they have described the pharmaceutical composition on pages 11-12 of the specification and that could be administered by any method recognized in the art. However, just listing a route does not provide how to practice a method. References of Anderson and Crystal cited in the previous office action have discussed the features of all the different vector systems in gene therapy and emphasize that any one vector or system may not be suitable for any method. It is emphasized that while progress has been made in recent years for *in vivo* gene transfer, vector targeting *in vivo* to desired organs continues to be unpredictable and inefficient. This is supported by numerous teachings available in the art. For example, Deonarain (1998) indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise, but is currently even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma et al. (published in 1997) reviews various vectors known in the art for use in gene therapy and the problems which are associated with each and clearly indicated that at the time of the claimed invention resolution to vector targeting had not been achieved in the art (see entire article). Verma discusses the role of the immune system in inhibiting the efficient targeting of viral vectors such that efficient expression is not achieved (see page 239 and 2nd and 3rd column of page 242. Verma also indicates that appropriate enhancer-promoter sequences can improve expression, but that the "search for such [useful] combinations is a case of trial and error for a given cell type" (page 240, sentence bridging columns 2 and 3). While applicants specification supports efficient transfer *in vivo* direct injection into the muscle, the specification fails to teach one of skill in the art how to overcome the unpredictability for vector targeting such that efficient gene transfer is achieved by any mode of delivery. The specification fails to teach any specific targeting techniques, fails to provide any working examples which encompass vector targeting, and fails to direct the skilled artisan to any teachings of targeting

strategies known in the art which would allow one of skill in the art to practice the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 24-45 rejected under 35 U.S.C. 102(b) as being anticipated by Triantaphyllopous et al (Arthritis & Reumatism 42:90-99, 1999).

This art teaches a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 91, results section on page 93-96 and figure 4).

Accordingly, this art anticipates the claimed invention of claims 24-45.

10. Claims 24-45 are rejected under 35 U.S.C. 102(B) as being anticipated by Triantaphyllopous et al (Gene Therapy 5:253-263, 1998).

This art teaches a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 259, left and right columns, results section on page 257, left column and discussion).

Accordingly, this art anticipates the claimed invention of claims 24-45.

11. Claims 24-45 rejected under 35 U.S.C. 102(b) as being anticipated by Croxford et al (The Journal of Immunology 160:5181-5187, 1998).

This art teaches a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 5182, left and right columns, results section on page 5182 right column to left column on 5185 and the discussion section).

Accordingly, this art anticipates the claimed invention of claims 24-45.

12. No claim is allowed.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.